The antibody was prepared as follows. Hybridoma L243 was grown and the culture supernatant collected using standard techniques [Harlow and Lane, eds., *Antibodies: A Laboratory Manual*, Cold Spring Harbor Press, New York (1988), pp. 272, 276]. Th monoclonal antibodies were purified from the hybridoma supernatants. L243 was purified on a Protein A-SEPHAROSE column (Pharmacia) using the protocol supplied by the manufacturer. The purified monoclonal antibody was then biotinylated using standard techniques [*Antibodies: A Laboratory Manual, supra* at p. 341]. Biotin was obtained from Vector. Biotinylated L243 was used at a dilution of 1:200.

Please add the following text on page 143, line 3:

We claim:

REMARKS

Claims 1-24 were originally filed in a parent case, while Claims 1-6 were elected for prosecution in this divisional application. Claims 25-32 were subsequently added, and Claim 2 was canceled in a Response to an Office Action dated December 19, 2000. Thus, Claims 1, 3-6 and 25-32 are currently at issue in the present application. In the Office Action dated July 30, 2002, the Examiner made a number of arguments and rejections.

Per the Examiner's request, Applicants note the sequence objection. Accordingly, a Request Under 37 C.F.R. § 1.821(e) To Use Computer Readable Form From Another Application is included herewith. The Applicants also note the claim informality objection and now amend the Specification to correct the error. Applicants also note the trademark objection and accordingly amend the Specification.

For clarity, the rejections at issue are set forth by number in the order they are addressed herein:

(1) The Amendment filed April 29, 2002 is rejected under 35 U.S.C. § 132 as allegedly constituting new matter.

(2) Claims 1, 3-6, and 25-32 are rejected under 35 U.S.C. § 112, paragraph one, as allegedly not being enabled.

(3) Claims 1, 3-6 and 25-32 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious in light of Tao et al. (362 Nature 755-758; hereinafter Tao), Stevenson et al. (in DNA Vaccines - A New Era in Vaccinology, Volume 72 Annals of the New York Academy of Sciences 212-226; hereinafter Stevenson), and de The (19 Blood Cells 667-675).

Applicants note that all amendments of the Specification presented herein are made without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG)[1] .

I. THE APRIL 29, 2002 AMENDMENT DOES NOT CONSTITUTE NEW MATTER

The amendment filed April 29, 2002 is objected to under 35 U.S.C. §132 as constituting new matter. The amendment states "...[a]n analogous approach for the treatment of T-cell lymphomas and leukemias would involve the production of a custom vaccine comprising autologous T cell receptor (TCR) idiotype which corresponds to the most abundant TCR molecule expressed on the surface of the *T-cell* tumor" (amendment italicized). See April 29, 2002 Office Action Response, p. 2. Support for this amendment is found within Example 10 of the Specification. Spec., pp. 88-103. In particular, the Specification states, "methods for the production of tumor-specific Ig derived from a B-cell lymphoma patient are provided. However, the general approach outlined herein is applicable for the production of tumor-specific proteins generally (i.e., production of soluble TCR for treatment of T cell

[1] 65 Fed. Reg. 54603 (Sept. 8, 2000).

tumors, production of Ig for treatment of B-cell leukemias, etc.)." Spec., p. 89. As such, the Applicants assert that the amendment does not constitute new matter and request that the objection be withdrawn.

II. THE CLAIMS OF THE PRESENT INVENTION ARE ENABLED

The Examiner rejects Claims 1, 3-6, and 25-30 under 35 U.S.C. §112, first paragraph, for not enabling multivalent vaccine compositions. The standard for determining whether a specification meets an enablement requirement is whether undue experimentation is needed to practice the invention. MPEP 2164.01. Several factors must be weighed by an examiner in making this assessment including the breadth of the claims, the nature of the invention, the state of the prior art, the level of one skilled in the prior art, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. MPEP 2164.01(a). A specification that discloses at least one method for making and using the claimed invention while bearing a reasonable correlation with the entire scope of the claim satisfies the enablement requirement. In re Fisher, 427 F2d 833, 839 (CCPA 1970). The Applicants submit that the present invention is enabled in the specification.

The Specification provides working examples and methods aimed at making multivalent vaccine compositions. Indeed, the Examiner admits that the specification is "enabling for a multivalent immunogenic composition." Office Action, p. 4. Yet, the Examiner also asserts that "[n]o guidance or working examples in the instant application have shown one of skill in the art how to use the claimed vaccines for the treatment or prevention of cancer." Office Action, p. 6. The Applicants respectfully disagree with the Examiner and assert that working examples and methods for making the claimed compositions are thoroughly provided in the Specification and Examples. In particular, the Specification at pages 51-55 extensively discusses the production of multivalent vaccines for the treatment of lymphoma and leukemia, and in-progress clinical trials. In addition, Example 10 (starting on

page 88 of the instant application) provides a working example for the production of multivalent vaccines used in the treatment of lymphoma and leukemia. Example 10 provides guidance in the construction of expression and selection/amplification plasmids, the collection of tumor cells, the isolation of RNA from tumor cells, the cloning of Ig genes from tumor cells, the expression and amplification of tumor-specific Ig in mammalian cells, the purification of tumor-specific Ig from amplified cell lines, and the administration of tumor-specific Ig multivalent vaccine. Spec., pp. 88-103. As such, the Specification and Examples provided in the present application provide ample guidance toward the creation of multivalent vaccine compositions.

The present invention provides working examples and methods for making multivalent vaccine compositions bearing reasonable correlation with the scope of the claims. The Examiner asserts that "because the art teaches that the efficacy of cancer vaccines is highly unpredictable, it would require undue experimentation by one of skill in the art to be able to practice the invention commensurate in scope with the claims." Office Action, pp. 6-7. The Applicants respectfully disagree. The present invention involves multivalent composition claims. The Specification provides a detailed description for making multivalent vaccine compositions. Spec., pp. 51-55. Example 10 provides experimental data from making multivalent vaccine compositions. Spec., pp. 88-103. The scope of Claims 1, 3-6, and 25-30 are aimed at multivalent vaccine compositions. As such, the correlation between the working examples and methods in the Specification and the Claims is more than reasonable.

The Examiner is respectfully reminded that methods of use are irrelevant in a composition claim under 35 U.S.C. §112. Methods of use are only applicable, to an extent at all, in 35 U.S.C. §101. The Examiner has made no §101 rejections. Indeed, the present application meets the §101 requirements because at least one required utility is provided (see Example 10).

III. THE CLAIMS ARE NOT OBVIOUS

The Examiner rejects Claims 1, 3-6, and 25-30 under 35 U.S.C. § 103. Applicants respectfully disagree and submit, in all cases, that the Examiner fails to provide a prima facie showing of obviousness as required under § 2143 of the MPEP. Prima facie obviousness requires 1) a suggestion or motivation in the references or the knowledge generally available to combine or modify the reference teachings; 2) the prior art must teach of a reasonable expectation of success should the suggested combination or modification take place; and 3) the prior art must teach or suggest all the claim limitations. A showing of obviousness will fail if any one of these elements is not met. Applicants submit that the present invention is nonobvious.

The present invention involves multivalent vaccine compositions that are not taught or suggested by the prior art. A finding of obviousness requires that all claim limitations be taught or suggested by the prior art. Here, each independent claim of the present invention teaches a multivalent vaccine composition with more than one idiotope. See Claims 1, 25, 28, 29 and 30. The Examiner urges that "Tao et al, Stevenson et al and de The teach of idiotypic immunogenic composition that are polyclonal." The Applicants respectfully disagree. Neither Tao et al nor Stevenson et al teach of a composition comprising more than one idiotope. Indeed, the Tao and Stevenson references teach away from creating a multivalent vaccine composition because, as the Examiner admits, these references "do not teach that lymphomas are polyclonal." Office Action, p. 7.

In addition, the de The reference does not teach or suggest creating multivalent vaccine compositions, or multivalent vaccine compositions with more than one idiotope. Rather, de The discusses the etiology of Burkitt's lymphoma, and states that the polyclonal B cell proliferation seen in Burkitt's lymphoma is the result of EBV infection. de The, pg. 670-672. Importantly, de The does not state or imply that Burkitt's lymphoma is <u>itself</u> polyclonal. In particular, neither the main de The reference or the discussion that follows contend that B cell lymphomas are multivalent in nature. Considering that this element of the present invention is not taught or suggested in the prior art, the Applicants respectfully request that the claim rejections be withdrawn.

The Federal Circuit has clearly stated that findings of motivation to combine prior art must be based on objective evidence of record, and not on hindsight reconstruction. In re Sang Su Lee, 277 F.3d 1338, 1342-43 (Fed. Cir. 2002). In addition, an examiner must make a showing of the teaching or motivation to combine prior art references. In re Dembiczak, 175 F.3d 994, 999 (Fed. Cir. 1999). Here, the Examiner asserts the present invention is obvious in light of Tao, Stevenson, and de The, and that the "art as taught by de The provides the motivation because de The discloses the multivalent mature (sic) of B-cell lymphomas and discloses possible avenues of treatment using such compositions." Office Action, pp. 7-8. The de The reference does not teach or even suggest multivalent vaccine compositions as a possible avenue of treating B-cell lymphomas. Rather, de The suggests vaccines against EBV as a possible means of reducing the incidence of Burkitt's lymphoma. de The, pg. 672. Furthermore, de The does not teach or suggest the use of vaccines comprising the idiotype of the lymphoma, whether univalent or multivalent, as a means of treating lymphomas. As such, de The provides no discussion of multivalent vaccine compositions. The Examiner is unable to provide the required showing of the teaching or motivation to combine prior art references. See in re Dembiczak. The Applicants reassert that the present invention is not motivated by prior art, and request that the claim rejections be withdrawn.

CONCLUSION

All grounds of rejection of the Office Action of July 30, 2002 having been addressed and reconsideration of the application is respectfully requested. It is respectfully submitted that the Claims should be allowed. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

Dated: December 30, 2002

Mary Ann D. Brow
Registration No. 42,363

PATENT
Attorney Docket No. **GENITOPE-03849**

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APPENDIX I

MARKED-UP VERSION REWRITTEN TEXT

PURSUANT TO 37 C.F.R. § 1.121(b)(1)(iii)

Please replace the paragraph beginning on page 79, line 14, with the following text:

The antibody was prepared as follows. Hybridoma L243 was grown and the culture supernatant collected using standard techniques [Harlow and Lane, eds., *Antibodies: A Laboratory Manual*, Cold Spring Harbor Press, New York (1988), pp. 272, 276]. The monoclonal antibodies were purified from the hybridoma supernatants. L243 was purified on a Protein A-[Sepharose] SEPHAROSE column (Pharmacia) using the protocol supplied by the manufacturer. The purified monoclonal antibody was then biotinylated using standard techniques [*Antibodies: A Laboratory Manual*, *supra* at p. 341]. Biotin was obtained from Vector. Biotinylated L243 was used at a dilution of 1:200.

Please add the following text on page 143, at line 3:

We claim: